08/372,676

**UNITED STATES DEPARTMENT OF COMMERCE**
**Patent and Trademark Office**
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| SERIAL NUMBER | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 08/372,676 | 01/17/95 | CHATTERJEE | M 434-047 |

| EXAMINER | |
|---|---|
| REEVES, J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1813 | 11 |

18N1/0313

LOWE PRICE LEBLANC AND BECKER
99 CANAL CENTER PLAZA
SUITE 300
ALEXANDRIA VA 22314

**DATE MAILED:** 03/13/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☑ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

**Part II SUMMARY OF ACTION**

1. ☑ Claims 1, 4-26 are pending in the application.
   Of the above, claims 5,6 are withdrawn from consideration.
2. ☐ Claims 2,3 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1, 4, 7-26 are rejected.
5. ☐ Claims _____ are objected to.
6. ☑ Claims 1-9 have previously been are subject to restriction or election requirement.
7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

**EXAMINER'S ACTION**

**Part III**

1. The Group and/or Art Unit location of your application in the PLO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1813.

2. Receipt of Amendment A, Paper No 7 filed 1/22/96 with a post card receipt date of 11/8/95, Supplemental Response, Paper No 8 filed 1/22/96 and Supplemental Amendment B, Paper no 10 filed 2/1/96 has been acknowledged. IN addition, an Examiner Interview Summary, Paper no 9 filed 1/25/96 has been placed in the file. It is noted that Amendment A, Paper No 7 states that "claims 5-8 have been withdrawn from consideration by the examiner" (page 2, last full paragraph), however, this is incorrect. As noted on page 3, paragraph 4, "claims 5-6 are withdrawn from consideration by the examiner" in Paper no 6, filed 8/9/95. Claims 2-3 have been cancelled. Claims 10-26 have been added. Claims 1, 4 7-9 have been amended. Claims 1, 4-26 are pending in the application. Claims 5-6 are withdrawn from consideration by the examiner as being drawn towards a non-elected invention.

3. Applicant's election with traverse of Group I (the antibody) and not group II (the method of treatment), in Paper No. 7 is acknowledged. The traversal is on the ground(s) that "because the compositions of the claims are similar, it is respectfully

submitted that the burden of search and examination of the entire application can be made without a serious burden" (see Paper No. 7, page 7, first paragraph). This argument is not persuasive. Further, applicant has provided no evidence to establish why the requirement for restriction is improper. As to the question of burden of search, the literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Further, it is doubted that applicant would readily accept the rejection of the process of the elected invention over a reference which relates only to the starting material. Clearly different searches and issues are involved in the examination of each group. Finally, the antibody product of group I can be used for more than one method, including the method of treatment in group II and the method of diagnosis suggested by claims 7-9. For these reasons the restriction requirement is deemed to be proper and is made **FINAL**.

4. This application contains claims 5-6 drawn to an invention non-elected with traverse in Paper No. 7. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (37 C.F.R. § 1.144) M.P.E.P. § 821.01.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in

compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

***Claim Rejections - 35 USC § 112***

6. The objection to the specification under 35 USC 112 first paragraph as set forth in paragraph 8 (bridging pages 5-6 of Paper no 6) and the rejections of the claims 1-4 and 7-9 have been withdrawn due to the clarification provided on pages 5-6 (Paper no 7) and the amendments to the specification.

7. The objection to the specification and claims 1, 4 and 7-9 are rejected under 35 USC 112 first paragraph as set forth in paragraph 9 (bridging pages 7-8 of Paper no 6) regarding the deposit of biological materials is withdrawn, due to the amendment of Paper 7 to the specification and due to the amendment of Claim 1 in Paper no 10.

8. Claims 1, 4 and 7-9 and newly added claims 10-26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention.

a. Claims 1 and 11 are vague and indefinite in reciting "having all the identifying characteristics of" as it is not clear what identifying characteristics are being claimed. Amending claim 1 to recite "the anti-idiotypic monoclonal antibody 1A7 produced by the hybridoma deposited under ATCC accession number HB-11786" would obviate this rejection.

b. Claim 10 is vague and indefinite in reciting "and progeny thereof" as it is not clear how the hybridoma cell line may be further developed over time and therefore, it is not clear what may be encompasses by this claim. In particular, it is not clear whether only the antibody producing progeny are claimed or whether the claim encompasses cells that no longer have the capability to produce the 1A7 antibody.

c. Claim 18 is vague and indefinite as it only recites one compound in the "composition". Compositions are made up of two or more compounds, such as an antibody and a pharmaceutically acceptable carrier.

d. Claim 26 is vague and indefinite for reciting monoclonal antibody 1A7 as this antibody name is merely a laboratory designation. Amending claim 26 to recite monoclonal antibody 1A7 produced by the hybridoma deposited under ATCC Accession no HB-11786" would obviate this rejection. Claim 26 is further considered to be vague and indefinite for reciting "an individual

treated with monoclonal antibody 1A7"and it is not clear when the individual was treated, i.e., subsequently, during or prior to when the sample was taken.

e. Claims 1, 4, 11, 12 and 18 are vague and indefinite as these claims contain limitations of equal scope with other claims. Claims 11 and 12 are duplicates of claim 1. Claim 18 is a duplicate of claim 4.

9. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to teach how to make and/or use the claimed invention, i.e., failing to provide an enabling disclosure.

10. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure.

a. The specification is silent concerning the treatment of humans with the complete and incomplete Freund's adjuvant, however, the broadly drawn claims encompass this possibility. It is well known in the immunology art that treatment of humans with

complete or incomplete Freund's adjuvant results in anaphylactic shock. In absence of evidence to the contrary, in view of the lack of guidance and/or working examples, one skilled in the art would not know how to be able to administer complete Freund's adjuvant to humans without encountering this problem.

11. Newly drawn claims 15 and 19 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

12. Claims 11, 12, 18 and 19 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 11-12 are essentially duplicative of Claim 1; Claim 18 is essentially duplicative of Claim 4; Claim 19 is essentially duplicative of Claim 15.

13. The objection to the specification under 35 USC 112 first paragraph as set forth in paragraphs 10-11 (bridging pages 9-10 of Paper no 6) and the rejections of claims 7-8 has been withdrawn in view of the amendment to claim 7.

14. The objection to the specification under 35 USC 112 first paragraph as set forth in paragraph 12 (bridging pages 10-11 of Paper no 6) and the rejection of the claim 9 has been withdrawn

in view of the amendment to the specification and upon further consideration.

***Claim Rejections - 35 USC § 102***

15. The rejection of claim 1 and newly drawn claims 10-12 under 35 USC 102(b) over Bhattacharya-Chatterjee et al 1993 is maintained.

a. Applicant's arguments concerning the enablement of the Bhattacharya-Chatterjee et al reference have been considered but are not found to be persuasive. In particular, Applicants argue that "the abstract lacks specific information and fails to provide an enabling disclosure of the invention. There is no way in the brief description presented in the abstract proves that the anti-idiotype antibody 1A7 (which is different from the 1A1-1A7 antibody discussed in the abstract) is an internal image of GD2" (page 10, first full paragraph). The Examiner maintains that the abstract fully teaches one skilled in the art how to make and use the claimed antibody. In particular, the Bhattacharya-Chatterjee et al. reference teaches the use of the "readily available" (paragraph bridging pages 13-14 of Paper no. 7) "murine mAb 14G2a antibody" "to generate monoclonal anti-Id antibodies (Ab2)" (see Abstract). The Bhattacharya-Chatterjee et al reference discloses that "[t]hree of the mAb2s reacted with the antigen binding site (paratope) of 14G2a, since they

inhibited the binding between $^{125}$I-labelled 14G2a and the target melanoma cell line M21-P6". Moreover, Bhattacharya-Chatterjee et al. disclose "monoclonal anti-idiotype antibodies", including "one of the clones, 1A1-1A7 has been used to raise anti-anti-Id antibodies (Ab3) in rabbits". The ability of the anti-idiotypic mAb 1A7 to generate an active immunity to GD2 antigen found on melanoma and small cell carcinoma of lung is an inherent property of the mAb 1A7.

b. In Paper No. 7, Applicant goes on to state that "Furthermore, the 1A1-1A7 antibody disclosed in the abstract is not identical to the 1A7 antibody proposed in the Patent application. Monoclonal antibody 1A7 has been obtained after many cycles of limiting dilution cloning of 1A1-1A7 and is truly monoclonal in nature."

c. This statement is clarified by the Supplemental Response (paper no 8 filed 1/22/96) in which Applicant discloses that the "preparation of antibodies prepared from the 1A1-1A7 cell line" was different from the "preparation of antibodies from the cell line deposited with the ATCC" (Paper no 8, page 1, second paragraph). Applicant has not provided evidence that the preparation of antibodies were actually different, but merely suggested that "it was therefore possible that the 1A1-1A7 cell line comprised contaminating cells. If the contaminating cells were immunoglobulin-producing cells, then any 1A7 preparation from the cells could comprise immunoglobulin from the

contaminating cells" (page 1-2 bridging paragraph). Further, applicant states that the "clonality of the cell line (and hence the stability of the line) may have been improved" (page 2, first full paragraph).

d. The specification states that "one of these clones 1AI-1A7 is used to raise anti-anti-idiotypic antibodies (Ab3) in rabbits" (Pages 11-12, bridging paragraph). Furthermore, the Bhattacharya-Chatterjee et al. reference teaches the generation of monoclonal antibodies, including the mAb2 1A1-1A7, are, by definition, clonal. It is not clear how the clonal 1A7 cell line could be further cloned to create a different monoclonal cell line 1A1-1A7. This argument is supported by Applicant's statement that the "recloning of the cell line is not expected to have affected the 1A7 producing cells comprised in the hybridoma described in the abstract" (Paper 8, page 2 second full paragraph). Therefore, the claimed 1A7 cell line is identical to the 1A1-1A7 cell line disclosed in the Bhattacharya-Chatterjee et al reference, and in absence of evidence to the contrary, as disclosure of the anti-Id-antibody 1A1-1A7, its method of production and its immunogenicity in rabbits occurred more than a year prior to the application date, issuance of a patent is barred.

e. It is noted that during the interview with Applicant's representatives on 25 January 1996, that Applicant indicated the

intention to submit declarations under 37 CFR 1.131/37 CFR 1.132 with evidence to affirm and/or demonstrate that

i). the antibody 1A7 was never made publically available more than one year prior to the publishing date, and

ii). the Chatterjee et al reference is not enabling, i.e., it does not teach how one skilled in the art would be able to make and/or use claims limited to the monoclonal antibody 1A7 produced by hybridoma deposited at ATCC under Accession number HB-11786 and having the particular amino acid sequence as discussed in the Interview on January 26 1996.

iii). that the 1A7 antibody as defined by its amino acid sequence is unique over the prior art.

Until this information has been submitted, the rejection of claim 1 and newly drawn claims 10-12 under 35 USC 102(b) over Bhattacharya-Chatterjee et al 1993 is maintained.

***Claim Rejections - 35 USC § 102(b)/103***

16. Claim 1 has been rejected under 35 USC 102(b) or in the alternative 35 USC 103 in view of Saleh et al (T) in the previous Office Action.

a. The rejection of claim 1 under 35 USC 102(b) is withdrawn in view of Applicant's arguments. in particular, Applicants indicate that the Saleh et al reference is not anticipatory as Saleh et al (T) teaches a human mouse hetero-

hybridoma producing monoclonal antibody IgG1 lambda specific for anti-GD-2 while the instant application claims a murine monoclonal antibody 1A7 of the IgG1 kappa subtype specific for anti-GD-2.

b. However, it is incumbent upon Applicant to produce an unobvious difference. Production of antibodies in rodents was well known and routinely used in the art at the time the claimed invention was made. Furthermore, it was well known in the art that when antibodies are made in rodents, one expects to obtain different isotypes having the same specificity, Applicant's only discernable differences between the claimed antibody and the Saleh et al's antibody is deemed to be an obvious variant in view of Saleh et al. In absence of evidence concerning the uniqueness of the 1A7 antibody, the rejection of claim 1 and newly added claims 10-12 under 35 USC 103 is maintained.

***Claim Rejections - 35 USC § 103***

17. The rejection of claims 1, 4, 7-9 and newly added claims 10-26 under 35 USC 103 over Mujoo et al. in view of Cheung et al is maintained.

a. Applicant argues that "Mujoo et al discloses IgG3 monoclonal antibodies produced against the neuroblastoma cell line NMB-7 GD2 antigen" and that these IgG3 monoclonal antibodies failed to show any activity in the presence of murine spleen

cells or complement (Paper No. 7, page 13, second paragraph). This is certainly true. However, as stated on pages 14-15 of Paper No. 6, Mujoo et al also disclose the anti-GD2 monoclonal antibody 14G2a which is identical to Applicant's immunogen. The 14G2a antibody was created by isotype switching of the IgG3 monoclonal antibody, as disclosed in the first and second sentences of the Abstract and is of the IgG2a isotype. Mujoo et al do not disclose or suggest the use of the 14G2a antibody to create anti-idiotypic antibodies.

b. Applicant argues that "Cheung et al disclose the monoclonal antibody 3F8 which is a murine IgG3 monoclonal antibody specific for GD2" (Paper No. 7, page 13, third paragraph). This is certainly true. However, as stated in the Paper no 6, page 14-15, Cheung also disclose the use of this anti GD antibody to make anti-Idiotype monoclonal antibodies that compete with the GD2 antigen and induce the production of anti-GD2 antibodies upon immunization into mice. Cheung et al disclose the production of 6 different anti-idiotype antibodies that compete with the GD2 antigen (see page 502, second column, first full paragraph). All six of the anti-idiotypic antibodies were of the IgG1 sub-class. In addition, as stated in the Paper no 6, pages 14-15, Cheung et al. provide motivation for the creation of anti-idiotypic (see first three sentences of the Abstract).

c. The Examiner respectfully asserts that Applicant is incorrect in arguing that "the prior art of record fails to provide any such suggestion or incentive to substitute the IgG1-k type antibody, as claimed for the IgG3 monoclonal antibodies of Cheung or Mujoo" (Paper No. 7, pages 13-14 bridging paragraph). As discussed above, Cheung et al disclose the creation of six different IgG1 anti-idiotypic antibodies specific for the GD2 antigen. Further, Applicant argue that "there is no motivation or reasonable expectation of success to use the readily available 14G2a monoclonal antibody of Mujoo et al. to produce anti-idiotypic antibodies that would generate active immunity against malignant melanomas and small cell carcinomas" (Paper No. 7, pages 13-14 bridging paragraph). As discussed above and in the earlier Office Action, Cheung et al provide motivation for one skilled in the art to want to make anti-idiotypic antibodies to the GD2 antibody as "the disialoganglioside GD2 is widely expressed among neuroblastomas, melanomas, small-cell carcinomas, sarcomas and brain tumors. Immunity directed against this antigen may have anti-tumor utility. Since GD2 is poorly immunogenic, anti-idiotypic antibodies may serve as alternative tumor vaccines" (see abstract). Therefore, in absence of any evidence demonstrating the uniqueness of the 1A7 antibody, this rejection is maintained.

18. No claim is allowed.

19. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Reeves, Ph.D., whose telephone number is (703) 308-7553. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christine Nucker, can be reached on (703) 308-4028. The fax phone number for this Group is (703) 305-7939. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

21. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PLO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Julie E Reeves

Julie E. Reeves, Ph.D.

(703) 308-7553

CHRISTINE M. NUCKER
SUPERVISORY PATENT EXAMINER
GROUP 180